CLAIMS

What is claimed is:

1. A method for creating a profile of interactions between components of at least one multicomponent biological complex for a sample, the method comprising, for each complex:

(a) providing an aliquot from the sample, wherein the aliquot comprises the multicomponent biological complex from the sample immobilized on a solid support through a biospecific affinity molecule, wherein the affinity molecule binds a first component of the complex and wherein unbound material has been removed from the solid support;

(b) washing the immobilized complex with a first sequence of elution washes, wherein the concentrations of a first solute in each elution wash in the sequence form a gradient of increasing or decreasing concentration; and

(c) measuring a second component in the successive elution washes;

whereby the profile for a complex from a sample comprises the measurements from the elution washes.

2. The method of claim **1** wherein the samples are selected from the group consisting of tissue extracts, cell extracts, blood, urine, lymphatic fluid, *in vitro* protein expression media and derivatives thereof.

3. The method of claim **1** wherein the at least one complex is one complex.

4. The method of claim **1** wherein the at least one complex is a plurality of complexes, each bound through a biospecific affinity reagent.

5. The method of claim **1** wherein the affinity molecule is selected from an antibody, a single chain antibody, a specific binding fragment of an antibody, an affibody, an enzyme, an enzyme substrate, a receptor, a receptor ligand, a drug, a nucleic acid, or an aptamer.

6. The method of claim **1** wherein the affinity molecule is immobilized to the solid support before binding the complex.

7. The method of claim 1 wherein the affinity molecule is bound to the solid support after binding the complex.

8. The method of claim 1 wherein the solid support is a chromatographic resin.

9. The method of claim 8 wherein the washes are performed in a non-flow-through device.

10. The method of claim 9, wherein the non-flow through device is a closed bottomed microtiter plate.

11. The method of claim 8 wherein the washes are performed in a flow-through device.

12. The method of claim 11 wherein the flow-through device is a microtiter drip plate, a flow-through column or a flow-through microcolumn.

13. The method of claim 1 wherein the solid support is a SELDI probe comprising the biospecific capture reagent for capturing the complex attached to a probe surface.

14. The method of claim 1 wherein the unbound material is removed with an initial wash.

15. The method of claim 1 wherein the solute is selected from an ion, a salt, a detergent, a biomolecule or a binding competitor.

16. The method of claim 1 comprising washing the immobilized complex in a second aliquot of the sample with a second sequence of elution washes, wherein the second solute is different than the first solute.

17. The method of claim 1 wherein the second component is detected by an optical method, an electrochemical method, atomic force microscopy or a radio frequency method.

18. The method of claim 1 wherein the second component is detected by mass spectrometry.

19. The method of claim **18** wherein mass spectrometry is affinity mass spectrometry.

20. The method of claim **19** wherein affinity mass spectrometry comprises SEND.

21. The method of claim **1** further comprising after step (b), measuring components of the complex still immobilized on the support through the biospecific affinity molecule, whereby the profile further comprises the measurements of the complex.

22. A method comprising:

a. providing a set of biological samples, wherein the set comprises at least two subsets, each subset characterized by a different biological characteristic;

b. creating a profile of interactions between components of at least one multicomponent biological complex for each sample in the set, wherein creating a profile for a complex for a sample comprises:

(i) providing an aliquot from the sample, wherein the aliquot comprises the multicomponent biological complex from the sample immobilized on a solid support through a biospecific affinity molecule, wherein the affinity molecule binds a first component of the complex and wherein unbound material has been removed from the solid supports;

(ii) washing the immobilized complex with a plurality of successive elution washes, wherein the concentrations of a solute in the successive elution washes form a gradient of increasing or decreasing concentration; and

(iii) measuring a second component in the successive elution washes, whereby the profile for a sample comprises the measurements from the elution washes solutions from each aliquot; and

c. comparing the profiles for the samples to detect differences in interaction between components in each subset.

23. The method of claim **22** wherein the different biological characteristics are selected from pathological v. non-pathological, drug responder v. drug non-responder,

toxic response v. non-toxic response and progressor to disease state v. non-progressor to disease state.

24. The method of claim **22** wherein the different biological characteristics are exposure to an inhibitor RNA or non-exposure to the inhibitory RNA.

25. The method of claim **22** wherein step (b) further comprises, after step (ii) detecting components of the complex still immobilized on the support through the biospecific affinity molecule, whereby the profile further comprises the measurements from the support.

26. The method of claim **22** comprising performing steps (b)(i)-(iii) on a second aliquot from the samples, wherein the elution washes comprise a second, different solute and the concentrations of the second solute in the successive elution washes form a gradient of increasing or decreasing concentration.

27. The method of claim **22** wherein comparing comprises using the profiles to train a computerized learning algorithm, wherein the computerized learning algorithm generates a classification algorithm that classifies a profile into one of the at least two subsets.

28. A method for creating a profile of interactions between components of at least one multicomponent biological complex for a sample, the method comprising, for each complex:

(a) providing a plurality of aliquots from the sample, each aliquot comprising the same multicomponent biological complex from the sample immobilized on a solid support through a biospecific affinity molecule, wherein the affinity molecule binds a first component of the complex and wherein unbound material has been removed from the solid supports;

(b) washing the immobilized complex in each of the aliquots with an elution wash from a first sequence of elution washes, wherein the concentrations of a first solute in the elution washes of the sequence form a gradient of increasing or decreasing concentration; and

(c) measuring at least one second component in each of the elution washes;

whereby the profile for a sample comprises the measurements from the elution washes from each aliquot.

29. The method of claim **28** further comprising after step (b), detecting components of the complex still immobilized on the support through the biospecific affinity molecule, whereby the profile further comprises the measurements from the support.

30. The method of claim **28** further comprising performing step (b) on a second plurality of aliquots from the sample, wherein the elution washes comprise a second, different solute and the concentrations of the second solute in the successive elution washes form a gradient of increasing or decreasing concentration.

31. A method comprising:

(a) providing a set of biological samples, wherein the set comprises at least two subsets, each subset characterized by a different biological characteristic;

(b) creating a profile of interactions between components of at least one multicomponent biological complex for each sample in the set, wherein creating a profile for a complex in a sample comprises:

(i) providing a plurality of aliquots from the sample, each aliquot comprising the same multicomponent biological complex from the sample immobilized on a solid support through a biospecific affinity molecule, wherein the affinity molecule binds a first component of the complex and wherein unbound material has been removed from the solid supports;

(ii) washing the immobilized complex in each of the aliquots with an elution wash of a first sequence of elution washes, wherein the concentrations of a first solute in the elution washes of the sequence form a gradient of increasing or decreasing concentration; and

(iii) measuring at least one second component in each of the elution washes;

whereby the profile for a complex in a sample comprises the measurements from the elution washes from each aliquot; and

(c) comparing the profiles for the samples to detect differences in interaction between components in the samples.

32. The method of claim **31** comprising washing the immobilized complex in a second plurality of aliquots from each sample with one elution wash of a second set of elution washes, wherein the concentrations of a second solute in each member of the set of

elution washes form a gradient of increasing or decreasing concentration, and wherein the second solute is different than the solute.

33. The method of claim **31** wherein step (b) further comprises, after step (ii) detecting components of the complex still immobilized on the support through the biospecific affinity molecule, whereby the profile further comprises the measurements from the support.

34. The method of claim **31** further comprising performing steps (b), (i)-(iii) on a second plurality of aliquots from the samples, wherein the elution washes comprise a second, different solute and the concentrations of the second solute in the successive elution washes form a gradient of increasing or decreasing concentration.

35. The method of claim **32** wherein comparing the profiles for the samples to detect differences in interaction between components in the samples

36. A kit comprising:

(a) at least one solid support having means to bind a first affinity molecule or to which a first affinity molecule is bound;

(b) at least one sequence of elution washes, wherein the concentrations of a first solute in each elution wash in each sequence form a gradient of increasing or decreasing concentration; and

(c) at least one MS probe, wherein the MS probe is different from the solid support.

37. The kit of claim **36** further comprising:

(d) at least one biospecific affinity molecule, wherein the affinity molecule specifically binds a first component of a first multicomponent biological complex.

38. The kit of claim **36** wherein the solid support is a chromatographic resin.

39. The kit of claim **36** further comprising a multiwell microtiter plate.

40. The kit of claim **39** wherein the microtiter plate is a drip plate.

41. The kit of claim **36** further comprising a column.

42. The kit of claim **41** wherein the column utilizes gravity flow, centrifugal flow or mechanically generated flow.

43. The kit of claim **36** wherein the MS probe is a SELDI probe comprising an adsorbent bound to the probe surface.

44. The kit of claim **36** wherein the MS probe is a MALDI probe.

45. The kit of claim **36** wherein the MS probe is a SELDI probe comprising an energy absorbing molecule bound to the probe surface.

46. The kit of claim **36** wherein the at least one MS probe is a plurality of MS probes.

47. The kit of claim **36** wherein the at least one MS probe comprises a plurality of SELDI probes comprising an energy absorbing molecule bound to the probe surface.

48. The kit of claim **36** wherein the at least one MS probe comprises a plurality of SELDI probes comprising an adsorbent bound to the probe surface.

49. The kit of claim **37** wherein the affinity molecule is selected from an antibody, a single chain antibody, a specific binding fragment of an antibody, an affibody, an enzyme, an enzyme substrate, a receptor, a receptor ligand, a drug, a nucleic acid, or an aptamer.

50. The kit of claim **37** wherein the at least one affinity molecule is a plurality of different affinity molecules and wherein each different affinity molecule specifically binds a first component of a different complex.

51. A kit comprising:

(a) at least a first MS probe which is a SELDI probe comprising a reactive surface, wherein the reactive surface can covalently couple a biospecific affinity molecule;

(b) at least one sequence of elution washes, wherein the concentrations of a first solute in each elution wash in each sequence form a gradient of increasing or decreasing concentration; and

(c) at least a second MS probe, wherein the MS probe is a MALDI probe or a SELDI probe comprising a chromatographic surface.

52. The kit of claim **51** further comprising:

(d) at least one biospecific affinity molecule, wherein the affinity molecule specifically binds a first component of a first multicomponent biological complex.

53. The kit of claim **52** wherein the affinity molecule is selected from an antibody, a single chain antibody, a specific binding fragment of an antibody, an affibody, an enzyme, an enzyme substrate, a receptor, a receptor ligand, a drug, a nucleic acid, or an aptamer.